

REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and the following remarks.

I. Status of the Claims

Claims 1-35 are currently pending in the application, with claims 1 and 10 being the independent claims.

Claims 1 and 10 are amended to specify that the plurality of animal cell colonies held in the medium are grown on the base of the sample container. Support for the amendment to claims 1 and 10 may be found, *inter alia*, in paragraph [0052] at page 4 of the published patent application.

Further, claims 1, 10 and 20-22 are amended to replace the term “lowering” with the term “moving”. Support for the amendment to claims 1, 10 and 20-22 may be found, *inter alia*, in Figure 12 of the published patent application.

These amendments do not introduce any new matter into the application and their entry is respectfully requested.

II. The Telephone Interviews with the Examiner

Applicants wish to thank Examiner Nathan Andrew Bowers for the courtesy extended to Applicants’ representative during the telephone interviews held on May 15 and May 17, 2007.

An amendment to claims 1 and 10 was proposed by the Examiner to put the application in condition for allowance. The amendment specified that, while in picking position, the distal end of the picking pin is offset from the animal cell colonies. After Applicants agreed to the amendment proposed by the Examiner, the Examiner objected to his own amendment stating that the amendment adds new matter into the application, since the application allegedly does not provide support for an offset distance of the pin from the animal cell colony during picking, but

rather refers to an offset distance from the container base. Applicants respectfully traverse this ground of rejection.

Applicants respectfully submit that both Figures 5 and 7 show that the colony is clearly offset from the end of the picking pin. Moreover, the exemplified quantitative distances between the distal end of the tip and the base, d_1 plus d_2 in Figure 7, (0.1 to 4 mm; 0.25 to 1 mm) would automatically result in an offset of the tip from the individual cells or colonies being picked (*see* specification at page 12, line 18 to page 13, line 3, and in particular lines 22, 23 and 28-30). In this respect, a typical cell has a diameter of about 20 microns. Therefore, when picking individual cells there would always be an offset between the top of the cell and the distal end of the tip. For example, even with the minimum exemplified base-tip offset of 0.1 mm, the tip-cell offset would be 0.08 mm. In the present application, the base-tip offset distance is typically chosen so that a tip-colony offset is preserved, since otherwise, as demonstrated at the personal interview with the Examiner held on October 12, 2006, the colony will be contacted by the tip and thus disrupted (*see* also Figure 7 and Figure 8B). The experimental evidence provided during the personal interview with the Examiner clearly showed that contact of the pin with the colony results in its destruction. The specification refers to the base as a reference for the offset from the tip because the control system must refer to a physically defined reference plane (*see* paragraph [0052] at page 4 of the published patent application).

In summary, the Office Action is incorrect in stating that the application does not disclose picking with a tip-to-colony/cell offset, since this is clearly illustrated in Figures 5 and 7. The exemplified values for the tip-to-base offset are sufficiently large that they necessarily imply that there will also be a tip-to-colony/cell offset. Although numerical values for the tip-to-colony/cell offset are not specifically disclosed in the specification, the disclosed numerical values for the tip-to-base offset disclose that a tip-to-colony/cell offset is to be maintained.

Accordingly, this rejection is improper. Reconsideration and withdrawal of this ground of rejection are therefore respectfully requested.

III. The Rejection Under 35 U.S.C. § 102

The Office Action, at pages 3-4, rejects claims 1, 2, 5, 6, 10, 18, 19, 21 and 22 under 35 U.S.C. § 102(e) as being allegedly anticipated by US Patent Application Publication No. 2003/0179916 A1 to Magnuson *et al.* (“Magnuson”). Applicants respectfully traverse this ground of rejection.

1. Summary of the Claimed Invention

The presently claimed invention is directed to a method for automated picking of animal cell colonies. The method employs a picking head comprising at least one hollow pin to pick the colonies. The method comprises moving at least one hollow pin to a colony picking position in which a distal end of the hollow pin is immersed in the medium and offset from the base of the sample container containing the animal cell colonies *by an offset distance* and aspirating the animal cell colony into the hollow pin *while the distal end of the hollow pin is held in the colony picking position*.

Further, the invention is directed to an apparatus for picking animal cell colonies comprising a camera for capturing images, a computer comprising an image processing software for identifying the location of the colonies and a control software for controlling the picking of the colonies by interacting with the image processing software, and a picking head comprising at least one hollow pin connected to a drive that introduces a distal end of the hollow pin into the sample container *offset from the animal cell colony*, such that the animal cell colonies are picked from the medium by the hollow pin *at an offset distance*. The control software of the computer controls the apparatus for colony picking by: (i) capturing an image of the animal cell colony with the camera; (ii) performing image analysis with the image processing software to detect animal cell colonies, thus creating a list of target colonies; and (iii) assigning the apparatus to collect the target colonies with the control software. The target colonies are picked by repeatedly

performing the following actions specified by the control software: (a) moving at least one hollow pin to an animal cell colony location in the pick list; (b) moving the hollow pin to a *colony picking position in which a distal end of the hollow pin is immersed in the medium and offset from the base of the sample container by an offset distance*, and (c) aspirating the animal cell colony into the hollow pin *while the distal end of the hollow pin is held in colony picking position*.

The invention is also directed to methods of using the apparatus for identifying and picking animal cell colonies.

The claimed methods and apparatus are specifically designed to pick animal cell colonies *while the distal end of the hollow pin is held in a picking position at an offset distance from the colonies during the picking procedure*, such that **no contact** is created between the picking pin and the cell colony, animal cell colonies are not destroyed and surrounding cell colonies are not displaced from their position.

2. The Cited Reference Fails to Teach Each and Every Element of the Claimed Invention

The Office Action states that Magnuson teaches that the hollow pin is aligned with the animal cell colony locations and that a distal end of the hollow pin is introduced into the cell medium proximate to the animal cell colony by an offset distance.

From these teachings, the Office Action then infers that, since the tip is only lowered to the colony, and since the colony must have a finite vertical extent above the base, Magnuson discloses lowering the end of the tip to a distance that is offset from the base of the container. The Office Action then concludes that Magnuson discloses a picking method that involves an offset between the end of the tip and the container base, as claimed in the present application.

Further, the Office Action, at page 12, alleges that "*there is no indication in Magnuson that the pin contacts the sample container base*" (see page 12, fourth and fifth lines from the

bottom). The Office Action's allegations, however, are not correct. In fact, Magnuson repeatedly states that in order to aspirate an adherent colony, the tip must either scrape the colony off the base prior to aspiration (*see* tip design as shown in Figure 3), or the tip must be sealed over the colony such that it can create a vacuum allowing the aspiration, i.e. sucking (*see* tip design as shown in Figure 4).

Specifically, Magnuson teaches that a tip can be designed for removal via aspiration techniques, such that it can form an essentially airtight seal with the colony or cell, or the tip can be designed for removal via a physical scraping motion, with a suitable scraping surface adapted to scrape a colony from the growth substrate (*see* paragraph [0127] at page 11 of Magnuson). These teachings may be additionally found throughout the specification in Magnuson (*see* paragraphs [0011], [0024], [0056], [0067], [0124-0127], [0160], [0169-0172], [0212]).

Magnuson's scraping tip shown in Figure 3 by definition involves contacting the tip with the container base, i.e. has zero offset from the base. Similarly, Magnuson's seal-and-suck alternative shown in Figure 4 also by definition involves contacting the tip with the container base, i.e. has zero offset from the base.

Magnuson teaches a seal such that during aspiration there is a sufficient pressure differential to dislodge the colony from the base, but for the tip to seal, the tip must necessarily be in contact with the base. Thus, in the methods provided by Magnuson the tip needs to be lowered down to the colony in order to aspirate it, and the aspiration is implemented using one of the two contact methods (i.e. scraping or airtight seal), which require zero offset from the base.

In summary, Magnuson fails to disclose or suggest an essential element of the claimed invention: Magnuson does not disclose or suggest a method and an apparatus for picking animal cell colonies, where animal cell colonies are picked and aspirated into the hollow pin *while the hollow pin is held in a colony picking position in which a distal end of the hollow pin is immersed in the medium and is at an offset distance from the base on which the colonies are grown*, such that there is ***no contact*** between the pin and the animal cell colony during the entire

picking procedure. Quite to the contrary, Magnuson teaches away from the claimed invention by requiring contact between the pin and the cell colony and failing to recognize that contact between the picking pin and the animal cell colony disrupts the cell colony and displaces surrounding colonies.

Thus, for at least the reasons stated above, this rejection is improper. Accordingly, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

IV. The Rejections Under 35 U.S.C. § 103

A. The Rejection Over Magnuson in view of Elverd

The Office Action, at pages 4-6, rejects claims 3, 13 and 33 under 35 U.S.C. § 103(a) as being allegedly unpatentable over U.S. Patent Application Publication No. 2003/0179916 A1 (“Magnuson”) in view of U.K. Patent Application No. 2310006 A (“Elverd”). Applicants respectfully traverse this ground of rejection.

The inability of Magnuson to teach or suggest the invention of claims 1-2, 5-6, 10, 18-19 and 21-22 is demonstrated above. The additional reference, Elverd, does not remedy the deficiencies of Magnuson. Rather, Elverd discloses a pneumatic actuator comprising an array of pistons that fire and retract individual pins that can collect and transfer biological samples. Thus, Elverd, like Magnuson, fails to disclose or suggest a method and an apparatus for picking animal cell colonies, where the colonies are picked and aspirated into the hollow pin while the hollow pin is held at an offset distance from the base on which the colonies are grown.

Accordingly, the rejection is improper. Therefore, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

B. The Rejection Over Magnuson in view of Sogi

The Office Action, at pages 6-7, rejects claims 4, 11-12 and 34-35 under 35 U.S.C. § 103(a) as being allegedly unpatentable over U.S. Patent Application Publication No.

2003/0179916 A1 (“Magnuson”) in view of U.S. Patent No. 4,210,724 (“Sogi”). Applicants respectfully traverse this ground of rejection.

The deficiencies of Magnuson in teaching or suggesting the claimed invention are demonstrated above. The additional reference, Sogi, does not remedy the deficiencies of Magnuson. Rather, Sogi is directed to an apparatus for liquid disposal and distribution for use in an automatic culture and fails to disclose or suggest a method and an apparatus for picking animal cell colonies, where the colonies are picked and aspirated into the hollow pin while the hollow pin is held at an offset distance from the base on which the colonies are grown.

Accordingly, the rejection is improper and its withdrawal is respectfully requested.

C. The Rejection Over Magnuson in view of Pareck

The Office Action, at pages 8-11, rejects claims 4, 7-9, 14-17, 20 and 27-28 under 35 U.S.C. § 103(a) as being allegedly unpatentable over U.S. Patent Application Publication No. 2003/0179916 A1 (“Magnuson”) in view of U.S. Patent No. 6,064,754 (“Pareck”). Applicants respectfully traverse this ground of rejection.

The inability of Magnuson in teaching or suggesting the claimed invention is demonstrated above. The additional reference, Pareck, does not remedy the deficiencies of Magnuson. Rather, Pareck is drawn to computer-assisted methods and apparatus for identifying, selecting and characterizing biomolecules in a biological sample. The reference fails to teach or suggest the non-contact picking method and apparatus claimed in the present application. Accordingly, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

D. The Rejection Over Magnuson

The Office Action, at page 11, rejects claims 23-26 and 29-32 under 35 U.S.C. § 103(a) as being allegedly unpatentable over U.S. Patent Application Publication No. 2003/0179916 A1 (“Magnuson”). Applicants respectfully traverse this ground of rejection.

As stated above, Magnuson clearly teaches that in order to aspirate an adherent colony, the tip must either scrape the colony off the base prior to aspiration (*see* tip design as shown in Figure 3), or the tip must be sealed over the colony so it can create a vacuum allowing the aspiration, i.e. sucking (*see* tip design as shown in Figure 4). Magnuson's scraping tip shown in Figure 3 by definition involves contacting the tip with the container base, i.e. has zero offset from the base. Magnuson's seal-and-suck alternative shown in Figure 4 also by definition involves contacting the tip with the container base, i.e. has zero offset from the base. Accordingly, Magnuson fails to teach or suggest the non-contact picking method and apparatus claimed in the present application. Therefore, the rejection is improper and its withdrawal is respectfully requested.

CONCLUSION

All of the stated grounds of rejections have been properly traversed or rendered moot. Therefore, the present application is now in condition for allowance, and an early notice to that effect is earnestly solicited.


The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. § 1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

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